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Applicant(s):	Turner *et al.*	Group Art Unit: 1647
Application No.:	09/771,961	Examiner: F. M. Hamud
Filed:	01/29/01	
Title:	Novel Human Membrane Proteins and Polynucleotides Encoding the Same	Atty. Docket No. LEX-0121-USA

APPEAL BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
Alexandria, VA 22313

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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on December 30, 2002. The Notice of Appeal was timely submitted on March 28, 2003, and was received in the Patent and Trademark Office ("the Office") on April 1, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of three months to and including September 1, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(2) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief (**$160.00**), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences.

III. STATUS OF THE CLAIMS

The present application was filed on January 29,2001, claiming the benefit of U.S. Provisional

Application Number 60/179,001, which was filed on January 28, 2000, and included original claims 1-4.

The First Official Action, was issued on July 02, 2002 ("the First Action"), claims 1-4 were rejected under 35 U.S.C. § 101 as allegedly lacking patentable utility, claims 1-4 were also rejected under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. Claims 1-2 were also rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite and under 35 U.S.C. § 102(b), as being allegedly being clearly anticipated by Hillier et al. (GenBank Accession no. AA399486).

In a response to the First Official Action, submitted to the Office on October 2, 2002 ("Response to the First Action"), Appellants amended claims 1 and 2 to further improve their clarity and new claims 5-8 were added to more particularly point out and distinctly claim the invention.

A Second and Final Official Action, was issued on December 30, 2002 (the "Final Action"), in which the rejection of claim 1 under 35 U.S.C. § 112 second paragraph was withdrawn, the rejection of claims 1-2 under 35 U.S.C. § 102(b) was withdrawn, the rejection of claims 1-8 under 35 U.S.C. § 101 as allegedly lacking a patentable utility was maintained and new claims claims 6-8 were rejectioned under 35 U.S.C. § 101 as allegedly being directed to non-statuatory subject matter, the rejection of claim 2 under 35 U.S.C. § 112 second paragraph was maintained and the rejection of claims 1-8 was maintained under 35 U.S.C. § 112, first paragraph, as allegedly one skilled in the art clearly would not know how to use the skilled invention.

In a response to the Final Action, submitted on April 30, 2003 ("Response to the Final Action"), claim 2 was amended and Appellants addressed in detail the outstanding rejections of claims 1-8.

An Advisory Action ("the Advisory Action") was mailed on July 15, 2003, the rejection of claim 2 under 35 U.S.C. § 112 was withdrawn, the rejection of claims 6-8 under 35 U.S.C. § 101 as allegedly being directed to a non-statutory subject matter was also withdrawn, rejection of claims 1-8 under 35 U.S.C. § 101 as allegedly lacking a patentable utility was maintained as was the rejection of claims 1-8 was also maintained under 35 U.S.C. § 112, first paragraph, allegedly as one skilled in the art clearly would not know how to use the skilled invention. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

Appellants believe that no additional outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode membrane proteins that are similar to CD receptor protiens, display four transmembrane regions as have been seen in similar proteins, such as CD82, and is most similar to CD63. The presently claimed invention was said to play a major role in cell cell interaction and signal transduction (specification at page 1, lines 23-24). The presently claimed polynucleotide sequences were compiled from clustered human gene trapped sequences and cDNA clones from human trachea, pituitary, and lung cDNA libraries (specification at page 15, lines 7-10). The specification details a number of uses for the presently claimed polynucleotide sequences, including the detection and for diagnosis, drug screening, clinical trial monitoring, the treatment of diseases and disorders, or cosmetic or nutriceutical applications (specification at page1, line 18-20) and to identify mutations associated with a particular disease and also as a diagnostic or prognostic assay (specification at page7, line 13-15) , as well as reagents in assays for screening for compounds that can be as pharmaceutical reagents useful in the therapeutic treatment of mental, biological, or medical disorders and disease (specification at page 15, lines 19-30). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page, line 29-318), particularly using a high throughput "chip" format (specification at page 5, line 4 through page 7 line 4), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions (specification at page 10, line 12-17), determining the genomic structure (specification at page 10, lines 11), and in diagnostic assays such as forensic analysis, human population biology and paternity determinations (see, for example, the specification from page 7, line 13-15).

VI. ISSUES ON APPEAL

1. Do claims 1-8 lack a patentable utility?

2. Are claims 1-8 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1-8 Lack a Patentable Utility?

The Final Action first rejects claims 1-8 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial utility or a well-established utility.

In a position first taken in the Final Action and maintained in the Advisory Action, the Examiner determined that the Appellants' position that credible evidence has been presented demonstrating that the sequences of the present invention are similar to CD proteins, such as CD82 and CD63, which are known to be cell surface receptors and mediators if cell-cell interaction and signal transduction is not persuasive.

In both the Final Action and the Advisory Action, Appellants' position was deemed non-persuasive allegedly because the sequence presented in the Response to the First Office Action as Exhibit E (now **Exhibit A**), allegedly does not have homology to SEQ ID NO2 of the present invention. Appellants respectfully submit that in fact the sequence provided in **Exhibit A,** International Protein Index No. IPI00083978 has homology a large degree of homology (100% over 216 of 248 amino acids) to SEQ ID NO2 of the present invention and that the Examiner is in error.

The Examiner's argument reiterates a point made in the Final Action, in which the Examiner submitted that SEQ ID NO:1 and 2 of the present invention are not related to CD proteins, such as CD82 and CD63, based on the Examiner's alleged finding that the instant sequences were identical to sequences of a published PCT application WO/200157213-A2 and that in this PCT application the sequences were identified as BCL-X like. In response Appellants had noted that this PCT application was no longer being pursued. Appellants now note and demonstrate that SEQ ID NOS:1 and 2 of the instant invention are not

the same as those in the published PCT application WO/200157213-A2 or those published by Guo, et al., 2001 (JBC, 276:2780-2785) and that the Examiner is in error. For simplicity only the amino acid sequences will be presented. The amino acid sequence of SEQ ID NO:2 of the instant case is:

"MLRNNKTIIIKYFLNLINGAFLVLGLLFMGFGAWLLLDRNNFLTAFDENNHFIVPIS QILIGMGSSTVLFCLLGYIGIHNEIRWLLIVYAVLITWTFAVQVVLSAFIITKKEEVQQLWHD KIDFVISEYGSKDKPEDITKWTILNALQKTLQCCGQHNYTDWIKNKNKENSGQVPCSCTK STLRKWFCDEPLNATYLEGCENKISAWYNVNVLTLIGINFGLLTSEVFQVSLTVCFFKNIK NIIHAEM".

While the amino acid sequence of the BCL-G protein described by Guo et al., 2001 is :

"MCSTSGCDLEEIPLDDDDLNTIEFKILAYYTRHHVFKSTPALFSPKLLRTRSLSQRGL GNCSANESWTEVSWPCRNSQSSEKAINLGKKKSSWKAFFGVVEKEDSQSTPAKVSAQG QRTLEYQDSHSQQWSRCLSNVEQCLEHEAVDPKVISIANRVAEIVYSWPPPQATQAGGFK SKEIFVTEGLSFQLQGHVPVASSSKKDEEEQILAKIVELLKYSGDQLERKLKKDKALMGHF QDGLSYSVFKTITDQVLMGVDPRGESEVKAQGFKAALVIDVTAKLTAIDNHPMNRVLGFG TKYLKENFSPWIQQHGGWEKILGISHEEVD".

Clearly these sequences are distinct. Therefore, the Examiner's argument, which was based on a false premise and a search using an incorrect sequence, can carry no weight.

As presented in Appellants' Response to the First Office Action, is the evidence of the credibility of Appellants assertion that the present invention is a human CD like membrane protein, similar to CD82 and CD63. Appellants submit results of a BLASTP analysis (**Exhibit B**) comparing SEQ ID NO: 2 and International Protein Index accession number IPI00083978.2 (GenBank Accession Nos. XP_084868/ XM__084868).

Appellants invite the Boards attention to the finding that the annotation on this IPI entry has changed from that which was submitted with earlier responses, whereupon it was annotated to be similar to CD82 antigen (Inducible Membrane Protein R2) (C33 Antigen) (IA4) (metastasis Suppressor Kangai 1) (Suppressor of Tumorgenicity-6). The annotation has now been changed by third party scientists, wholly

unaffiliated with Appellants, to read as *Homo sapiens* (Human) similar to CD63 antigen. Although this would appear to suggest confusion as to the identity of the protein, it does not confuse Appellants' position that the sequences of the present invention encode human CD-like membrane proteins, as both CD82 and CD63 would be recognized by those of skill in the art to be CD like membrane proteins.

Also included as **Exhibit C** is a BLASTN analysis comparing the nucleic acid sequence of SEQ ID NO:1 with GenBank Accession No. XM_084868 also now annotated by third party scientists, wholly unaffiliated with Appellants, as *Homo sapiens* (Human) similar to CD63 antigen. Included as **Exhibit D** is the GenBank description of description of Accession Nos. XM_084868 and XP_084868.

Given this clear and convincing evidence that those of skill in the art would recognize the present invention as a membrane CD-like membrane proteins, similar to CD82 and CD 63, clearly there can be no question that Appellants' asserted utility for the described sequences is "credible." Appellants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the sequences of the present invention encodes a membrane protein similar to CD proteins, such as CD82 and CD63 and has all the recognized utility thereof. As such, the scientific evidence clearly establishes that Appellants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101.

The Final Action argues that Appellants have not disclosed a physiological role for said protein. However, Appellants have asserted that the polypeptide is a novel CD-like human membrane protein and in Section 2 of the specification disclosed that such membrane proteins play important roles as, *inter alia*, mediators of cell-cell interaction and signal transduction. It is Appellants' position that patentable utility is distinct from, and does not require a knowledge of, physiological function. In fact, historically patentable utility has not required a knowledge of how the invention functions. It is also Appellants' position that unless Applicant is claiming a physiological function, evidence of a physiological function is not required to demonstrate patentable utility and that structural claims, such as those of the present application, are sufficiently supported by structural disclosure as defined by 35 U.S.C. § 101 and related case law. Appellants' assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Appellants' asserted utility.

The Advisory Action discounts Appellants' position that utility can be distinct from physiologic function. Appellants respectfully disagree and submit, for example, that many enzymes are used in commercial processes, a clear utility that is distinct from their physiologic role. In addition, as described in the present case nucleic acid can have utilities, as specific and substantial markers of identity when used, for example, in forensic analysis, that are separate from their physiologic roles. Thus, it is clear that a nucleic acid or amino acid sequences can be "useful" in many ways that are non-physiologic and therefore a knowledge of the physiologic role, while clearly of scientific interest, is not essential to patentable utility. On such utility is when the presently claimed polynucleotides can be used in DNA chips.

The Examiner admits that the presently claimed polynucleotides can be used in DNA chips, but states that this is a generic use (Advisory Action at page 7). Further, the Examiner seems to be requiring Appellants to "identify the biological role of the nucleic acid or function of the protein encoding the nucleic acid (*sic*)" (the Advisory Action at page 5-7) before the present sequences can be used in gene chip applications that meet the requirements of § 101. Appellants respectfully point out that knowledge of the exact function or role of the presently claimed sequence **is not required** to track expression patterns using a DNA chip. As set forth in Appellants' Response to First Action, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome, and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details at least on page 5, lines 26-29. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit E**), 5,556,752 (**Exhibit F**), 5,744,305 (**Exhibit G**), as well as more recently issued U.S. Patent Nos. 5,837,832 (**Exhibit H**), 6,156,501 (**Exhibit I**) and 6,261,776 (**Exhibit J**). Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful. Additionally, since only a small percentage of the genome (2-4%) actually

encodes exons, which in-turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications, further discounting the Examiner's position that such uses are "generic". Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

The sequences of the present invention describes human membrane proteins similar to CD proteins, such as CD82 and CD63, has been annotated by others as *Homo sapiens* similar to CD63 antigen (XM_084868), and provide a unique identifier of the corresponding gene. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using DNA chips.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit K**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit L**). Clearly, the usefulness of human genomic data, such as the presently claimed

nucleic acid molecule, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

However in the Advisory Action, the Examiner states that the present sequences fail to comply with the requirements of § 101 because "Without a disclosure of a particular disease state ...it would be impossible to determine what the results of a gene expression monitoring assay mean." (the Advisory Action at page 6). And yet, this is the very basis of much of DNA chip analysis, differential expression of specific sequences, which may or may not represent a particular gene are examined for differential expression in normal and diseased tissue. Thus the sequences of the present invention which represent a specific gene, encoding a membrane protein similar to CD 63, which is expressed in certain tissues (human cell lines, human trachea, prostate, testis, thyroid, salivary gland, small intestine, skeletal muscle, heart, uterus, mammary gland, adipose, esophagus, cervix, pericardium, hypothalamus, ovary, and fetal lung cells, and gene trapped human cells) and not others (as described in the final paragraph on page 2 of the specification) has particular value in such forms of analysis. In addition, this position as applied to the presently claimed sequences is wholly unsupported by mandatory legal precedent, since it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 309 F.2d 769, 135 USPQ 311 (CCPA, 1962). Furthermore, in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under

35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. The Examiner states that the present sequences do not meet the requirements under § 101 because "further testing" (the Final Action at page 3) would be required. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Rather, regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at

748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)).

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the sequences to a specific region of a human chromosome, as described in the specification at least at page10, lines 12-17. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually **any** other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

As discussed above, only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Appellants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Appellants' position, the Board is

requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

As further evidence supporting Appellants' submitted information localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions, evidence was provided in the Appellants' Response to Final Action as Exhibit C (now **Exhibit M)**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 9 exons spread non-contiguously along a region of human chromosome 12,at approximately 12q21. which are contained within partially overlapping clones, AC135034.1, AC025418.23 and AC135034.1. Thus clearly one would not simply be able to identify the 13 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Such genomic localizations are used, *inter alia*, in establishing the genetic role in disease processes by tracking familial associations.

While not reiterated in the Final Office Action, the First Action cited an article by Skolnick, Fetrow and Kolinski ("Skolnick et al."; 2000, Nature Biotechnol **18**:283-7) as evidence that one cannot assign function to a protein based on overall structure or domain family (page 4) and that this allegedly supports a lack of utility in the present case. However, Skolnick *et al.* state that"Whereas the goal of converting protein structure into function can be accomplished by traditional sequence motif-based approaches, recent studies have shown that assignment of a protein's biochemical function can also be achieved by scanning its structure for a match to the geometry and chemical identity of a known active site. And conclude that "When applied to genomes, structural information (either experimental or predicted) is likely to play an important role in high-throughput function assignment". Clearly Skolnick *et al.* believe such information has great value. In the present case this argument is rendered moot by the fact that the sequences of the

present invention are essentially identical to protein recognized by those of skill in the art to be a CD protein. Appellants have provided several pieces of evidence that those of skill in the art would find Appellants' assertion credible. That evidence clearly shows that those of skill in the art, in no way affiliated with Appellants, when faced with the same information, would and did identify the sequences of the present invention as a human membrane protein similar to CD proteins such as CD82 and CD63. Thus those of skill in the art agree with Appellants' assertion and would, therefore, clearly find Appellants' assertion credible. Given the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable, this is clear evidence that those skilled in the art would have recognized the function and activity of the protein encoded by the sequences of the present invention, there can, therefore, be no question that Appellants' asserted utility for the described sequences is "credible." According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

Furthermore, with regard to the citation of journal articles to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely the latest examples. Appellants agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Appellants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is **not the standard** for patentability under 35 U.S.C. § 101. Appellants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the

invention to be **believable**. Appellants submit that the overwhelming majority of those of skill in the relevant art would **believe** prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by extensive number of journal articles (which support Appellants' assertion that the overwhelming majority of those of skill in the art place a high value on prediction of protein function from homology information and the usefulness of bioinformatic predictions), and would thus **believe** that Appellants sequence is a CD-like membrane protein, similar to CD87 and CD63 . As **believability** is the standard for meeting the utility requirement of 35 U.S.C. § 101, and **not** 100% consensus or 100% accuracy, Appellants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101. Even the **PTO itself** does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials only requires a similarity score greater than 95% to establish functional homology (pages 53-55; **Exhibit N**). Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Appellants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as irrelevant to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility.

Finally, while Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit O**), 5,654,173 (**Exhibit P**), and 5,552,281 (**Exhibit Q**; each of which claims

short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit R**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants agree that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law. Appellants, therefore, submit that the rejection of claims 1-8 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1-8 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1-8 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in **Section VIII(A)** concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana*, *supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1-8 have been shown to have "a specific, substantial, and credible utility", as detailed in **Section VIII(A)** above, the present rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. An isolated nucleic acid molecule comprising the nucleotide sequence described in SEQ ID NO: 1.

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions including washing in 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence shown in SEQ ID NO:2.

4. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.

5. An expression vector comprising a nucleic acid sequence of Claim 3.

6. A cell comprising the expression vector of Claim 5.

7. An expression vector comprising a nucleic acid sequence of Claim 4.

8. A cell comprising the expression vector of Claim 7.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1-8 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

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